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**New Kind of Experimental HIV Vaccine Might Solve Key Problem in AIDS Battle**

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A new kind of experimental HIV vaccine protected some monkeys from getting sick with AIDS and suggests a potential solution to one of the most vexing dilemmas facing AIDS-vaccine makers. But the way the experiment was designed leaves some critical questions unanswered.

The study, being reported in this month's edition of the scientific journal *Nature Medicine*, is important because it tackles a key problem: Can a vaccine be designed to generate antibodies powerful enough to neutralize HIV, the AIDS virus? Classic vaccines, such as those for polio and measles, work by prodding the body to make such antibodies, which snare the virus and render it incapable of infecting cells.

But making antibodies that neutralize HIV has proved to be very difficult. Most of the antibodies generated by past vaccines either don't disable HIV at all or only neutralize one particular strain. Because HIV is one of the most mutable viruses known, a single infected person typically harbors a swarm of different strains.

A research team led by veteran AIDS researcher Anthony Fauci, who heads the National Institute of Allergy and Infectious Diseases, and Giuseppe Scala of Niaid and the University of Catanzaro in Italy, believe they have taken a significant, albeit preliminary, step in addressing this problem.

Some experimental AIDS vaccines, including one in human trials made by VaxGen Inc. of Brisbane, Calif., work by eliciting antibodies. But in recent years, the field has moved toward trying to stimulate another arm of the immune system, called killer T-cells, that scientists believe is also crucial to controlling HIV. Merck & Co., Whitehouse Station, N.J., reported earlier this year that it is conducting human trials of an experimental vaccine that incites such killer T-cells, and researchers at Harvard University, Yale University, Emory University and the National Institutes of Health have developed similar vaccines. These killer T-cell vaccines kept animals from getting sick and dying when exposed to HIV-like viruses, but scientists believe that, to be truly effective, a successful vaccine might also need to produce antibodies.

The study published today tries to stimulate antibodies that would work against a broad range of HIV strains. One way of stimulating antibodies is to inoculate a person with fragments of the virus itself. Confronted with such virus particles, the body thinks it is under attack with the real HIV and produces antibodies.

But this study used a relatively new strategy. The researchers deployed protein particles called peptides that resemble certain key parts of HIV. Interestingly, these peptides weren't taken from HIV itself but from wholly unrelated viruses called phages that infect bacteria.

These phages were engineered to produce millions of random peptides. By painstakingly screening these peptides in test-tube studies, the researchers found a few that reacted with HIV antibodies, suggesting they might be useful in a vaccine.

Four out of five monkeys vaccinated with the peptides produced antibodies -- and when those four animals were later injected with a virulent AIDS virus, none of them got sick from the disease. By contrast, seven control monkeys all got sick or died.

While that sounds impressive, some researchers noted that the study didn't completely rule out whether the peptide vaccine stimulated other arms of the immune system, such as killer T-cells or the so-called helper cells that orchestrate various immune responses. "It could be antibodies conferring this mild protection, but

it's not entirely clear because other immune responses weren't thoroughly examined," said David Montefiori, an expert in HIV antibodies and a professor at the Center for AIDS Research at Duke University.

What's more, an important statistical analysis didn't include the one vaccinated monkey in which the vaccine failed to stimulate antibodies. Deleting that monkey from the statistical analysis made the results seem more promising. And no matter how the data are analyzed, the results aren't as strong as those published in some of the studies using vaccines that stimulate killer T-cells, said several experts in the field.

Still, despite these caveats, using the peptides from the phages represents "a potentially very exciting way to solve the problem," said Prof. Montefiori. "It deserves to be looked at further."

Dr. Fauci defended his study. "The heavy weight of evidence says that antibody is the major player," he said, adding that various statistical methods validated the main findings.

Separately in the same journal, researchers from Germany said they have illuminated one of the strategies HIV uses to escape the immune system, a finding that may help in developing new treatments.

The researchers found that a protein within HIV, called nef, short-circuits the mechanism by which cells infected with viruses usually kill themselves. Such cell suicide, called apoptosis, is a way for the body to protect itself by eliminating cells that viruses have invaded. But the nef protein in HIV, which disrupts many immune-system functions, blocks the cell-suicide function, thereby keeping the cell -- and HIV -- alive.

In a third study also being published in Nature Medicine today, researchers from Italy and the U.S. found that human herpes virus 6, or HHV-6, gums up one of the molecular locks that HIV uses to enter cells. HHV-6 causes cells to release a molecule called Rantes that in turn attaches to a receptor called CCR5 that is on cell surfaces. HIV uses CCR5 to enter the cell, but it can't do so when Rantes has already attached to it.

The rub is that HIV can also use another receptor, called CXCR4, to get into cells -- and the strain of HIV that uses this other receptor is more virulent, causing sickness and death sooner. So by blocking CCR5, HHV-6 may force HIV to mutate into a more virulent form.

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Region	All Regions
Language	English
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Timestamp	23 February 2019 2:42 PM